Cognitive impairments and subjective cognitive complaints after survival of cardiac arrest

Resuscitation 120 (2017) 132–137

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Cognitive impairments and subjective cognitive complaints after survival of cardiac arrest: A prospective longitudinal cohort study

Catherine V.M. Steinbusch[a], Caroline M. van Heugten[b,c,*], Sascha M.C. Rasquin[a], Jeanine A. Verbunt[a,d], Véronique R.M. Moulaert[a,d]

[a] Adelante, Centre of Expertise in Rehabilitation and Audiology, Zandbergsweg 111, 6432 CC Hoensbroek, The Netherlands
[b] School for Mental Health and Neuroscience, Department of Psychiatry and Neuropsychology, Faculty of Health, Medicine and Life Sciences, Maastricht University, PO box 616, 6200 MD, Maastricht, The Netherlands
[c] Department of Neuropsychology and Psychopharmacology, Faculty of Psychology and Neuroscience, Maastricht University, PO box 616, 6200 MD, Maastricht, The Netherlands
[d] CAPHRI School for Public Health and Primary Care, Department of Rehabilitation Medicine, Maastricht University, PO box 616, 6200 MD, Maastricht, The Netherlands

ARTICLE INFO

Article history:
Received 21 May 2017
Received in revised form 16 July 2017
Accepted 5 August 2017

Keywords:
Cardiac arrest
Cognitive functioning
Cognitive complaints

ABSTRACT

Background: Cardiac arrest can lead to hypoxic brain injury, which can affect cognitive functioning.
Objective: To investigate the course of objective and subjective cognitive functioning and their association during the first year after cardiac arrest.
Methods: A multi-centre prospective longitudinal cohort study with one year follow-up (measurements at two weeks, three months and one year). Cognitive functioning was measured with a neuropsychological test battery and subjective cognitive functioning with the Cognitive Failures Questionnaire.
Results: 141 cardiac arrest survivors participated. Two weeks post cardiac arrest 16% to 29% of survivors were cognitively impaired varying on the different tests, at three months between 9% and 23% and at one year 10%–22% remained impaired with executive functioning being affected most. Significant reduction of cognitive impairments was seen for all tests, with most recovery during the first three months after cardiac arrest. Subjective cognitive complaints were present at two weeks after cardiac arrest in 11%, 12% at three months and 14% at one year. There were no significant associations between cognitive impairments and cognitive complaints at any time point.
Conclusions: Cognitive impairments are common in cardiac arrest survivors with executive functioning being mostly affected. Most recovery is seen in the first three months after cardiac arrest. After one year, a substantial number of patients remain impaired, especially in executive functioning. Because of absence of associations between impairments and complaints, cognitive testing using a sensitive test battery is important and should be part of routine follow-up after a cardiac arrest.

Introduction

Cardiac arrest (CA) can lead to ischemic-hypoxic brain injury with subsequent cognitive deficits varying from mild to severe and affecting different domains of cognitive functioning [1–14]. Most reported deficits are loss of memory, psychomotor deficits and problems in executive functioning [1–14]. At three months post arrest, Ørbo concluded that 44% in a cohort of 45 survivors were cognitively impaired to some degree [8]. Tiainen et al. [13] investigated cognitive performance of CA survivors at six months post arrest. Of 41 survivors, 34% had mild to moderate cognitive deficits and 17% had severe cognitive deficits. Cognitive deficits were predominantly detected in executive and memory functions [13]. Further research at one year concluded that a substantial number of patients had cognitive deficits, with memory being mostly affected in up to 64% [14]. Most recovery of deficits occurs in the first three months [10,12,14,15]. Large heterogeneity between studies and differences in assessment instruments make it difficult to draw firm conclusions about the incidence of cognitive impairments and their time course after surviving CA, which emphasizes the necessity of the current study.

* Corresponding author at: Faculty of Psychology and Neuroscience, Maastricht University, PO box 616, 6200 MD, Maastricht, The Netherlands.
E-mail address: caroline.vanheugten@maastrichtuniversity.nl (C.M. van Heugten).

http://dx.doi.org/10.1016/j.resuscitation.2017.08.007
0300-9572/

Besides cognitive impairments, subjective cognitive complaints can be present. Previous research has shown that at four weeks after CA 10 of 77 (13%) survivors had subjective cognitive complaints [16]. In this study, it is remarkable that the overlap between patients with cognitive impairments and those with cognitive complaints was limited (<30%), which raises questions about the relation between objective and subjective cognitive functioning. Another study used the Global Deterioration Scale to detect self-estimated cognitive deficits six months post arrest, with 56% of survivors rating themselves as having some degree of cognitive deficits [17]. At three years after CA, Wachelder et al. showed that 13 of 61 (21%) survivors had subjective cognitive complaints [18]. Research on patients with stroke and mild traumatic brain injury has shown no or only a mild correlation between cognitive complaints and cognitive impairments [19,20]. To our knowledge this relationship has not been studied in CA survivors yet. Previous research shows that cognitive problems can negatively affect quality of life, participation and autonomy of survivors [5,10,15,18,21,22].

In the present study the scope was twofold. The first goal was to examine cognitive impairments and subjective cognitive complaints and their course up to one year after CA. The second goal was to examine whether subjective cognitive complaints and objective cognitive impairments were associated.

Methods

A. Design

This study was part of the larger project 'Activity and Life after survival of a Cardiac Arrest' (ALASCA) [ISRCTN74835019]. The ALASCA project consisted of a multi-center prospective longitudinal cohort study (n = 238) with a nested randomized controlled trial (RCT, n = 185) to evaluate the effectiveness of a new nursing intervention [22]. To evaluate natural recovery of cognition after CA, we excluded patients randomized into the intervention group of the RCT from the analysis of the current study. This resulted in a cohort of 141 patients who received care as usual, best reflecting natural recovery. Patients were followed for one year with measurements at two weeks, three months and twelve months after CA.

B. Setting

Patients were recruited from coronary care and intensive care units of seven hospitals in the Netherlands, between April 2007 and December 2010. All hospitals had protocols for care of resuscitation patients in line with international guidelines and performed induced hypothermia and pacemaker implantations.

C. Participants

Patients who survived an in- or out-of-hospital CA, aged 18 years or older, admitted to a participating hospital, living within a 50 km range from the hospital with sufficient knowledge of Dutch language were included. Exclusion criteria were life expectancy of less than three months due to another medical condition and patients living in residential or institutional care prior to CA.

D. Procedure

Newly admitted survivors of CA were assessed for eligibility and potential participants were approached between three and ten days after CA. Patients who decided to participate signed an informed consent form. If the patient did not have the capacity to consent, the caregiver was asked for provisional consent. Baseline measurements were performed within two weeks (=T1) with further assessments at three months (=T2) and one year (=T3). All measurements were performed at the patients current location by research assistants who were trained to administer the tests and questionnaires and were done with the patient, not by proxy. This study complies with the Declaration of Helsinki and has been approved by the Medical Ethics Committee of Maastricht University Medical Centre and the local committees of the participating hospitals.

Table 1
Cognitive test battery and dependent measures for each test.

Test	Domain(s)	Dependent measure(s)
Cog-Log	Global cognitive performance	Total correct
TMT-A	Psychomotor functioning	Time in seconds
TMT-B	Executive functioning	Time in seconds
Verbal Fluency	Semantic memoryWord fluency	Total correct
PR Direct	Short-term memory	Total correct
PR Delayed	Delayed memory	Total correct
AMIPB	Information processing speed	Total correct

Cog-Log = Cognitive Log, total score; TMT = Trail Making Test (part A/part B), time in seconds; PR = Paragraph Recall (direct/delayed), number of total recalls; AMIPB = The Adult Memory and Information Processing Battery, number of correct answers; CFQ = Cognitive Failures Questionnaire, total score.

E. Assessment

1. Cognitive functioning

Cognitive functioning was assessed using a neuropsychological test battery to cover different cognitive domains as shown in Table 1. The battery included the following tests: Cognitive-Log (global cognitive performance) [23], Trail Making Test A (psychomotor functioning) and B (executive functioning) [24], Verbal Fluency Test (semantic memory and word fluency) [25], Paragraph Recall (PR) Test Direct and Delayed (short-term and delayed verbal memory) [26] and The Adult Memory and Information Processing Battery (AMIPB) Task A (information processing speed) [27]. For all tests except the Cog-Log and the AMIPB Task A, population-based age, gender and education-corrected normative scores were available [28]. Cognitive impairments were defined as a score below 1.5SD of published population norms. For the Cog-Log, a cut-off score of <25 was used to define cognitive impairment [23]. For the AMIPB, no normative data were available. Therefore, we did not define a cut-off score but only show the raw data.

2. Subjective cognitive functioning

The presence of subjective cognitive failures was assessed using the Cognitive Failures Questionnaire (CFQ). The CFQ is a 25-item questionnaire with a maximum score of 4 for each question leading to a total maximum score of 100. Participants with scores above 44 were considered to have subjective cognitive complaints [29].

3. Statistical analyses

Statistical analyses were performed using the SPSS 24 IBM software package. Data were checked for normality. Descriptive statistics were used to present baseline characteristics, presented by mean (SD) or median (range) for numerical variables, and number (%) for categorical variables. Median (range) scores on the cognitive tests and the CFQ are presented and the number of corresponding percentages of survivors with cognitive impairments or complaints according to the fixed cut-off points were calculated. To determine whether there was a significant improvement on the cognitive tests and subjective cognitive complaints over time, we performed non-parametric Friedman testing with an additional separate post-hoc-Wilcoxon signed rank test. Associations between cognitive impairments and cognitive complaints were determined by calculating Spearman correlations at T1, T2 and T3. Results were considered significant at $p < 0.05$.

Results

A. Patient characteristics

Table 2 shows the baseline demographic and disease characteristics of the 141 included patients; 84% were male, mean age was 60 years (SD ± 11), 85% was married or living with a partner, 81% had a high education level, 51% had a paid job prior to the CA. Most patients had an out-of-hospital CA (79%) with witnesses (94%) and bystander CPR (88%). The median time of collapse to return of spontaneous circulation was 10 min. Most patients returned home after their admission to the hospital (89%). Two survivors did not have the capacity to consent, so their caregivers were asked for provisional consent until the patient had the capacity to decide. For the complete project the percentage of patients that refused to participate was 29%, and the main reasons for refusing were lack of time/too much burden, lack of interest and medical problems.

From the 141 patients included for this study, 31 (22%) patients did not complete the study as shown in Fig. 1. There were no significant differences between participants who dropped out during the study and those who completed it regarding age (p = 0.242), gender (p = 0.515), location of the CA (p = 0.414), immediate start of CPR (p = 0.110) and level of education (p = 0.168). In contrast, those who dropped out during the study had a lower initial score on all cognitive tests at two weeks (range p < 0.001 to p = 0.033) except for the CFQ (p = 0.813). At three months (T2), there were no significant differences on all cognitive tests (p = 0.058 to p = 0.164) except for the AMIPB task A (p = 0.028).

Baseline assessments were performed on average after 24 days (SD11), with 3- and 12-months follow-up assessments on average after 98 days (SD15) and 374 days (SD15), respectively. The different sample sizes for the cognitive tests are based on the numbers of patients who completed the tasks.

B. Cognitive functioning

Table 3 presents the results of the cognitive tests. At two weeks after the CA overall cognitive functioning (Cog-Log) was impaired in 26%, psychomotor functioning in 25% (TMT-A) and executive functioning in 29% (TMT-B). Semantic memory and word fluency were impaired in 29% (TMT-B), short-term verbal memory in 19% (PR direct) and delayed verbal memory in 16% (PR delayed). At 3 months, the percentage of patients with impairments in overall cognitive functioning was reduced to 15%, and at one year to 13% (Cog-Log). After one year, psychomotor functioning remained impaired in 21% (TMT-A), executive functioning in 22% (TMT-B).

Table 2
Socio-demographic and medical characteristics.

	n	n (%) or mean (SD) or median (range)
Socio-demographical variables		
Male	141	119 (84%)
Age in years	141	60 (11)
Marital status	130	
- Married/partner		110 (85%)
- Single/divorced/widowed		20 (15%)
Highest level of education	130	
- Basic education		25 (19%)
- Further education		79 (61%)
- Higher education[a]		26 (20%)
Employment status pre-arrest	138	
- Paid job		70 (51%)
- Not working		68 (49%)
Medical history	135	
Cardiovascular history		
- Hypertension		41 (30%)
- Myocardial infarction		45 (33%)
- Heart failure		8 (6%)
- Cardiac arrest		2 (1%)
- CABG		11 (8%)
- Arrhytmia		10 (7%)
No cardiovascular history		51 (38%)
Diabetes mellitus		13 (10%)
Neurological history		20 (15%)
Characteristics cardiac arrest		
- Cardiac cause	132	117 (89%)
- Location out-of-hospital	141	112 (79%)
- Witnessed cardiac arrest	138	130 (94%)
- Bystander CPR	137	121 (88%)
- Initial cardiac rhythm VF/VT	124	117 (94%)
- Time collapse–ROSC, minutes	62	10 (0–60)
Medical interventions		
- Therapeutic hypothermia	135	63 (47%)
- Catheterisation with PCI	133	44 (33%)
- CABG	135	20 (15%)
- ICD	134	34 (25%)
- Pacemaker	135	7 (5%)
Characteristics after cardiac arrest		
Duration coma, in days	102	1 (0–19)
Location of discharge	129	
- Home		114 (89%)
- Rehabilitation centre		12 (9%)
- Nursing home		3 (2%)

CABG = Coronary Artery Bypass Graft; CPR = Cardiopulmonary Resuscitation; VF = Ventricular Fibrillation; VT = Ventricular Tachycardia; ROSC = Return Of Spontaneous Circulation; PCI = Percutaneous Coronary Intervention; ICD = Implantable Cardioverter Defibrillator.

[a] Refers to professional education or university.

Table 3
Objective and subjective cognitive impairments at two weeks (T1), three months (T2) and one year (T3).

	T1			T2			T3			
Test	n	Median (range)	No. (%) impaired	n	Median (range)	No. (%) impaired	n	Median (range)	No. (%) impaired	Change over time
Cog-Log[1]	129	26 (7–30)	34 (26%)	118	27 (19–30)	18 (15%)	107	27 (15–30)	14 (13%)	p = 0.004[a,c]
TMT-A[2]	126	44 (19–135)	31 (25%)	118	40 (14–183)	27 (23%)	107	37 (15–150)	22 (21%)	p = 0.003[c]
TMT-B[2]	121	113 (37–629)	35 (29%)	116	100 (32–433)	25 (22%)	105	87 (27–600)	23 (22%)	p = 0.010[a]
Verbal Fluency[1]	128	17 (7–37)	27 (21%)	118	20 (5–40)	14 (12%)	106	21 (9–47)	11 (10%)	p < 0.001[a,c]
PR direct[1]	129	6 (0–14)	24 (19%)	116	7 (1–14)	11 (10%)	105	7 (1–15)	16 (15%)	p = 0.030[a]
PR delayed[1]	129	4 (0–12)	21 (16%)	117	6 (0–13)	11 (9%)	105	6 (0–14)	10 (10%)	p < 0.001[a,c]
AMIPB[1]	128	28 (7–52)	–	117	30 (4–55)	–	105	32 (7–52)	–	p < 0.001[a,c]
CFQ[2]	103	23 (0–68)	11 (11%)	107	23 (0–69)	13 (12%)	97	26 (0–78)	14 (14%)	p = 0.027[c]

1 = Higher scores indicate better performance.
2 = Higher scores indicate worse performance.
Cog-Log = Cognitive Log, total score; TMT = Trail Making Test (part A/part B), time in seconds; PR = Paragraph Recall (direct/delayed), number of total recalls; AMIPB = The Adult Memory and Information Processing Battery, number of correct answers; CFQ = Cognitive Failures Questionnaire, total score.
Change over time:
a = significant difference between first and second measurement.
b = significant difference between second and third measurement.
c = significant difference between first and third measurement.

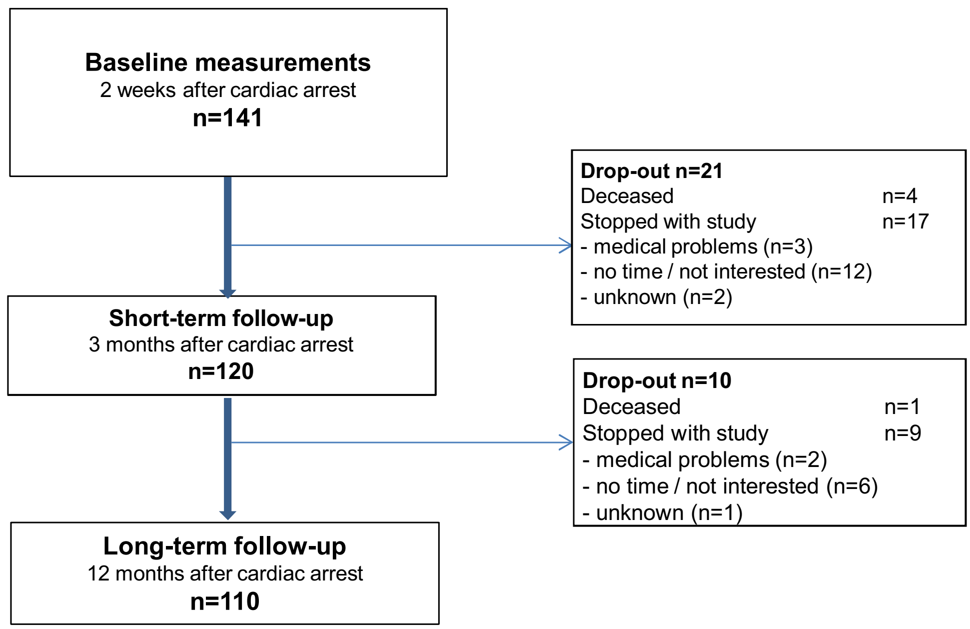

Fig. 1. Patient Flowchart.

Table 4
Number of cognitive tests impaired at two weeks (T1), three months (T2) and one year (T3).

Number of tests impaired	T1 n (%)	T2 n (%)	T3 n (%)
0	53 (46%)	64 (57%)	59 (57%)
1–2	39 (34%)	35 (31%)	33 (32%)
3–4	21 (18%)	12 (11%)	7 (7%)
5–6	3 (2%)	1 (1%)	4 (4%)

Short-term verbal memory remained impaired in 10% (PR direct), delayed verbal memory in 15% (PR delayed) of patients one year after CA. Significant reduction of cognitive impairments was seen for all tests. Most recovery was seen within the first three months after CA. Table 4 shows the distribution of impairments. At two weeks 54% of survivors were impaired in one or more tests, at 3 months and 12 months 43%.

At two weeks after CA 11% of survivors experienced subjective cognitive complaints, at three months 12% and at one year 14%. Subjective cognitive complaints increased significantly over time ($p = 0.027$).

C. Associations between cognitive impairments and cognitive complaints

Table 5 presents the correlation analyses between cognitive tests and cognitive complaints and shows that there are no significant associations at any time point.

Discussion

This study shows that a substantial number of CA survivors suffer from cognitive impairments with executive functioning being affected most. Subjective cognitive complaints are limited and there is no significant relation between experienced complaints and actual impairments.

In comparison to our results, a recent study that also used extensive neuropsychological tests in a cohort of 45 survivors three months after CA showed that 31% scored below cut-off on one or two tests, and 13% had three and more average test scores below cut-off with fine-motor functioning, memory, attention and executive functions being significantly impaired. 56% of survivors scored within the normal range on all cognitive tests [8]. A recent study from van Alem et al. shows comparable results at six months post CA ($n = 57$) with impairments ranging from 11% on divided attention, mental flexibility and motor speed to 28% on selective attention and response inhibition. Fifty-eight percent scored unimpaired at all tests [11]. Our study showed comparable results with a substantial number of patients without impairments, or poor performance in one or two tests which might indicate milder impairments. When regarding the fact that 89% of our cohort were discharged home after hospital admittance, many survivors had to cope with (mild) cognitive problems at home. Especially the survivors with less obvious, milder cognitive impairments should receive health workers attention and examination of cognition while their impairments might easily go unrecognized and may negatively influence return to former social roles, participation, return to work and quality of life [10,15,18,22,30,31].

We should take into account that our results of the objective cognitive tests at two weeks post CA might be overestimated while the dropped-out patients scored significantly worse on all tests at two weeks post CA. At three months there was no significant difference detected anymore except for one test (AMIPB task A).

In line with previous research, our study has shown significant recovery on all tests with most improvement occurring in the first three months following CA [10,15]. Although most cognitive recovery was seen within the first three months, most cognitive tests except for direct memory (verbal fluency test) and executive functioning (TMT-B) showed ongoing significant improvement between three and twelve months suggesting a longer period of recovery and a delayed plateau. In future research, adding more time points could help to establish differential recovery patterns for different cognitive functions and individual differences in recovery potential [14].

In the current study 11% of survivors had cognitive complaints at two weeks post CA. Interestingly, subjective cognitive complaints increased significantly over time. This might be explained by the fact that survivors become aware of their impairments when more complex cognitive functioning is being addressed when returning to daily functioning and occupation [21]. It is interesting to note that the patients in the current study showed percentages of cogni-

Table 5
Correlations between objective cognitive test scores and subjective cognitive complaints at two weeks (T1), three months (T2) and one year (T3).

	T1			T2			T3		
Test	n	Rs CFQ	p	n	Rs CFQ	p	n	Rs CFQ	p
Cog-Log	101	−0.093	0.356	106	0.024	0.806	95	−0.015	0.884
TMT-A	102	0.037	0.711	107	0.034	0.726	95	−0.011	0.278
TMT-B	98	−0.046	0.651	106	0.083	0.396	94	0.094	0.376
Verbal Fluency	101	−0.064	0.523	107	−0.079	0.428	94	−0.092	0.377
PR direct	101	−0.083	0.409	105	0.017	0.866	93	−0.093	0.376
PR delayed	101	−0.063	0.530	106	0.012	0.907	93	−0.059	0.571
AMIPB	101	−0.157	0.116	105	−0.088	0.370	93	−0.148	0.158

Rs = Spearman correlation; CFQ = Cognitive Failures Questionnaire; Cog-Log = Cognitive Log, total score; TMT = Trail Making Test (part A/part B), time in seconds; PR = Paragraph Recall (direct/delayed), number of total recalls; AMIPB = The Adult Memory and Information Processing Battery, number of correct answers; CFQ = Cognitive Failures Questionnaire, total score.

tive complaints comparable to the research of Boyce et al. [16], but lower percentages than the abovementioned studies with stroke and mild traumatic brain injury patients [19,20]. Clinical experience leads to similar observations and a possible explanation could be that having survived a CA makes people grateful that they survived which may reduce the level of complaints or believe their deficits belong to a normal ageing process. Another possible explanation could be the fact that the deficits found do not interfere with daily life when extensive cognitive functioning is not being addressed. From a neurological point of view it would be interesting to know whether this lack of complaints could be due to diminished awareness of deficits. Caregiver information is valuable when detecting cognitive problems in CA survivors while caregivers tend to report more changes as compared to the patients themselves and may be a more realistic representation of actual deficits [30].

The second aim of our study was to investigate the relationship between objective and subjective cognitive functioning. Our results have shown only a weak non-significant relation between cognitive impairments and cognitive complaints. This has been shown in other forms of brain injury as well such as stroke and mild traumatic brain injury [19,20], and has consequences for follow-up assessments. It is therefore important to identify patients with cognitive impairments by using objective cognitive tests while it is likely that patients will not complain about their cognitive problems.

Early neuropsychological assessment is recommended even in patients with apparent good outcome and those without cognitive complaints [31]. A recent report of Lilja suggests performing screening at 2 months post arrest [32]. In case of cognitive problems, referral to cognitive rehabilitation is recommended [31,32]. For patients with other forms of acquired brain injury, cognitive rehabilitation has been proven to be effective [33,34]. There are no studies yet on the effectiveness of cognitive rehabilitation specifically for patients with hypoxic brain injury due to CA. Comparable to patients with other types of acquired brain injury, we expect that CA survivors with cognitive deficits may benefit from cognitive rehabilitation interventions in terms of learning to compensate for probably lasting cognitive impairments. In addition, attention should be paid to anxiety and depression as they often co-occur with cognitive impairments, are related to cognitive complaints and also influence outcome of rehabilitation [14,16,18]. Recently, the 'Stand still and move on' intervention which we developed and evaluated in our RCT was shown to be clinically- and cost-effective and useful by both patients and health workers [22,35]. The intervention led to a higher quality of life and better emotional functioning after one year [22].

Strengths and limitations

This is the first large-scale cohort study in which cognitive impairments were measured with neuropsychological tests in combination with subjective cognitive measurements in a longitudinal design. A limitation of this study is the fact that the used neuropsychological tests have not yet been validated specifically for survivors of CA. Although all tests are valid for use in patients with acquired brain injury and have good test-retest reliability, it might be possible that some aspects of cognitive functioning in this group were over- or underestimated. Except for the paragraph recall test, patients received the same tests at every testing moment with a possible training effect. Additionally, the use of cut-offs creates a simplified, dichotomous result that may not accurately characterize impairments. A survivor who is consistently in the impairment range but above cut-off may go unrecognized.

Most cardiac arrests were witnessed, of cardiac cause and with initial shockable registered cardiac rhythm and with bystander CPR. It is affirmed that OHCA survivors who receive CPR from a bystander or an emergency medical provider, and these who are found in shockable rhythm are associated with better cognitive functioning [36]. Therefore, a possible selection bias might have occurred. Forty-seven percent of survivors were treated with therapeutic hypothermia and had a median of one day of coma duration. Both hypothermia treatment and shorter coma duration are associated with better outcome [2,8]. There might have been an inclusion bias regarding the fact that no patients in vegetative state have been included in the current study, possibly explained by the fact that their family members did not approve participation in a critical situation, which might overestimate cognitive functioning in our study group.

Furthermore, future studies should include data on pre-morbid cognitive functioning as cognitive decline might be caused by cardiovascular morbidity as well as being a result of the CA [1].

Conclusions

A substantial number of CA survivors suffer from cognitive impairments and subjective cognitive complaints. Regarding these cognitive impairments, this study shows that executive functioning seems to be mostly affected. Most recovery was seen in the first three months post injury with further recovery on some tests. After one year a substantial number of patients remained impaired. Subjective cognitive complaints do not seem to be indicative for actual cognitive impairments; therefore, cognitive testing with an extensive test battery as well as asking survivors and their caregivers about experienced subjective impairments is important and should be part of CA survivors routine follow-up to detect those survivors in need of cognitive rehabilitation programs.

Conflict of interest statement

None declared.

Funding

This work was supported by the Netherlands Organisation for Health Research and Development (ZonMw 920-03-373); Fonds Nuts Ohra (0602-069) and Stichting Elisabeth Strouven. The funding agencies were not involved in the design, performance or interpretation of the study.

Acknowledgements

We would like to acknowledge all patients for their participation in this study. We thank all participating hospitals, involved staff members and research assistants.

References

[1]. Lilja G, Nielsen N, Friberg H, et al. Cognitive function in survivors of out-of hospital cardiac arrest after target temperature management at 33 °C vs 36 °C. Circulation 2015;131:1340–9.
[2]. Alexander MP, Lafleche G, Schnyder D, Lim C, Mieke V. Cognitive and functional outcome after out of hospital cardiac arrest. JINS 2011;17:364–8.
[3]. Sulzgruber P, Kliegel A, Wandaller C, et al. Survivors of cardiac arrest with good neurological outcome show considerable impairments of memory functioning. Resuscitation 2015;88:120–5.
[4]. Alnes Buanes E, Gramstad A, Kjellsdotter Søvig K, et al. Cognitive function and health-related quality of life four years after cardiac arrest. Resuscitation 2015;89:13–8.
[5]. Mateen FJ, Joseph KA, Trennery MR, et al. Long-term cognitive outcomes following cardiac arrest. Neurology 2011;77:1438–45.
[6]. Torgerson J, Strand K, Bjelland TW, et al. Cognitive dysfunction and health-related quality of life after a cardiac arrest and therapeutic hypothermia. Acta Anaesthesiol Scand 2010;54:721–8.
[7]. Sabedra AR, Kristan J, Raina K. Neurocognitive outcomes following successful resuscitation from cardiac arrest. Resuscitation 2015;90:67–72.
[8]. Ørbo M, Aslaksen PM, Larsby K, et al. Determinants of cognitive outcome in survivors of out-of-hospital cardiac arrest. Resuscitation 2014;85:1462–8.
[9]. Andersson AE, Rosén H, Sunnerhagen KS. Life after cardiac arrest: a very long term follow up. Resuscitation 2015;91:99–103.
[10]. Moulaert VR, Verbunt JA, van Heugten CM, Wade DT. Cognitive impairments in survivors of out-of-hospital cardiac arrest: a systematic review. Resuscitation 2009;80:297–305.
[11]. van Alem AP, de Vos R, Schmand B, Koster RW. Cognitive impairment in survivors of out-of-hospital cardiac arrest. Am Heart J 2004;148(3):416–21.
[12]. Sauve MJ, Walker JA, Massa SM, Winkle RA, Scheinman MM. Patterns of cognitive recovery in sudden cardiac arrest survivors: the pilot study. Heart Lung 1996;25:172–81.
[13]. Tiainen M, Poutiainen E, Oksanen T, et al. Functional outcome, cognition and quality of life after out-of-hospital cardiac arrest and therapeutic hypothermia: data from a randomized controlled trial. Scand J Trauma Resusc Emerg Med 2015;6(23):12.
[14]. Lim C, Verfaellie M, Schnyer D, Lafleche G, Alexander MP. Recovery, long-term cognitive outcome and quality of life following out-of-hospital cardiac arrest. J Rehabil Med 2014;46(7):691–7.
[15]. Ørbo M, Aslaksen PM, Larsby K, Schäfer C, Tande PM, Anke A. Alterations in cognitive outcome between 3 and 12 months in surivors of out-of-hospital cardiac arrest. Resuscitation 2016;105:92–9.
[16]. Boyce-van der Wal LW, Volker WG, Vliet Vlieland TPM, van den Heuvel DMJ, van Exel HJ, Goossens GH. Cognitive problems in patients in a cardiac rehabilitation program after out-of-hospital cardiac arrest. Resuscitation 2015;93:63–8.
[17]. Cronberg T, Lilja G, Rundgren M, Friberg H, Widner H. Long-term neurological outcome after cardiac arrest and therapeutic hypothermia. Resuscitation 2009;80:19–123.
[18]. Wachelder EM, Moulaert VRMP, van Heugten C, Verbunt JA, Bekkers SCAM, Wade DT. Life after survival: long-term daily functioning and quality of life after an out-of-hospital cardiac arrest. Resuscitation 2009;80:517–22.
[19]. Duits A, Munnecom T, van Heugten C, van Oostenbrugge RJ. Cognitive complaints in the early phase after stroke are not indicative of cognitive impairment. J Neurol Neurosurg Psychiatry 2008;79:143–6.
[20]. Stulemeijer M, Vos PE, Bleijenberg G, van der Werf SP. Cognitive complaints after mild traumatic brain injury: things are not always the way they seem. J Psychosom Res 2007;63:637–45.
[21]. Bunch TJ, White RD, Smith GE, et al. Long-term subjective memory function in ventricular fibrillation out-of-hospital cardiac arrest survivors resuscitated by early defibrillation. Resuscitation 2004;60:189–95.
[22]. Moulaert VR, van Heugten CM, Winkens B, et al. Early neurologically-focused follow-up after cardiac arrest improves quality of life at one year: a randomized controlled trail. Int J Cardiol 2015;193:8–16.
[23]. Alderson AL, Novack TA. Reliable serial measurement of cognitive processes in rehabilitation: the Cognitive Log. Arch Phys Med Rehabil 2003;84(5):668–72.
[24]. O'Donnell WE, Reynolds DM, De Soto CB. Neuropsychological impairment scale (NIS): initial validation study using trailmaking test (A&B) and WAIS digit symbol (scaled score) in a mixed grouping of psychiatric, neurologic, and normal patients. J Clin Psychol 1983;39(5):746–8.
[25]. Vlaar AM, Wade DT. Verbal fluency assessment of patients with multiple sclerosis: test-retest and inter-observer reliability. Clin Rehabil 2003;17(7):756–64.
[26]. Sunderland A, Watts K, Baddeley AD, Harris JE. Subjective memory assessment and test performance in elderly adults. J Gerontol 1986;41(3):376–84.
[27]. Vlaar AM, Wade DT. The Adult Memory and Information Processing Battery (AMIPB) test of information-processing speed: a study of its reliability and feasibility in patients with multiple sclerosis. Clin Rehabil 2003;17(4):386–93.
[28]. Schmand B, Houx P, de Koning I. Normen van psychologische tests voor gebruik in de klinische neuropsychologie. Sectie Neuropsychologie Nederlands Instituut van Psychologen 2012.
[29]. Broadbent DE, Cooper PF, FitzGerald P, Parkes KR. The cognitive failures questionnaire (CFQ) and its correlates. Br J Clin Psychol 1982;21(Pt1):1–16.
[30]. Cronberg T, Lilja G, Horn J, et al. Neurologic function and health-related quality of life in patients following targeted temperature management at 33 °C vs 36 °C after out-of-hospital cardiac arrest. JAMA neurol 2015;72(6):634–41.
[31]. Ørbo M, Aslaksen PM, Larsby K, et al. Relevance of cognition to health-related quality of life in good-outcome survivors of out-of-hospital cardiac arrest. J Rehabil Med 2015;47(9):860–6.
[32]. Lilja G. Follow-up of cardiac arrest survivors: why, how, and when? A practical approach. Semin Neurol 2017;37(1):88–93.
[33]. van Heugten C, Gregório GW, Wade D. Evidence-based cognitive rehabilitation after acquired brain injury: a systematic review of content of treatment. Neuropsychol Rehabil 2012;22(5):653–73.
[34]. Brands I, Custers M, van Heugten C. Self-efficacy and quality of life after low-intensity neuropsychological rehabilitation: a pre-post intervention study. NeuroRehabilitation 2017;40(4):587–94.
[35]. Moulaert VR, Goossens M, Heijnders IL, Verbunt JA, van Heugten CM. Early neurologically focused follow-up after cardiac arrest is cost-effective: a trial-based economic evaluation. Resuscitation 2016;106:30–6.
[36]. Nichol G, Guffey D, Stiell IG, et al. Post-discharge outcomes after resuscitation from out-of-hospital cardiac arrest: a ROC PRIMED substudy. Resuscitation 2015;93:74–81.